[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS

ACTION: Notice

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 209 and 37 CFR Part 404 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-

7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

SUPPLEMENTARY INFORMATION: Technology descriptions follow.

Rabbit Antisera to Various Matrix, Matricellular, and Other Secreted Proteins

Description of Technology: The extracellular matrix (ECM) is composed of a group of proteins that regulate many cellular functions, such as cell shape, adhesion, migration, proliferation, and differentiation. Deregulation of ECM protein production or function contributes to many pathological conditions, including asthma, chronic obstructive pulmonary disease, arthrosclerosis, and cancer. Scientists at the NIH have developed antisera against various ECM components such as proteoglycan, sialoprotein, collagen, etc. (http://www.nidcr.nih.gov/Research/NIDCRLaboratories/CranioSkeletal/Antisera.htm). These antisera can be used as research tools to study the biology of extracellular matrix molecules.

Potential Commercial Applications: Studying the biology of extracellular matrix molecules.

Development Stage: Early-stage

Inventor: Larry Fisher (NIDCR)

Intellectual Property: HHS Reference No. E-135-2008/0 - Research Tool. Patent protection is not being pursued for this technology.

Licensing Contact: Sally Hu, Ph.D., M.B.A.; 301-435-5606; hus@mail.nih.gov

Collaborative Research Opportunity: The National Institute for Dental and Craniofacial Research is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize antibodies for studying the biology of extracellular matrix molecules. For collaboration opportunities, please contact David Bradley, Ph.D. at bradleyda@nidcr.nih.gov.

mNFHcre Transgenic Mice

Description of Technology: Knockout mouse is a valuable model to study biological functions of target genes. When Cre expressing mice are bred with mice containing a loxP-flanked gene, the gene between the loxP sites will be deleted in the offsprings. Scientists at the NIH have generated mNF-H-*cre* transgenic mouse lines that express Cre recombinase under the control of the promoter of the neurofilament-H gene, which is expressed in the late stage of neuronal maturation. The transgenic mice express *cre* in neurons (but not astrocytes) with highest expression in the cortex and hippocampus. The mNF-H-*cre* transgenic mouse line can be used to generate conditional knockout mice with targeted excision of neuron-specific genes during the late stage of mouse development. This mouse model will be useful for the study of neuronal functions of particular genes.

Potential Commercial Applications: Generating conditional knockout mice for neurobiological, neuro-developmental, or aging studies involving neurons of the brain and the spinal cord.

Competitive Advantages: Transgenic mice express Cre recombinase selectively in neurons (but not in astrocytes) in the late stage of brain development.

Development Stage: In vivo data available (animal)

Inventor: Ashok Kulkarni (NIDCR)

Publications:

1. Hirasawa M, et al. Neuron-specific expression of Cre recobinase during the late phase of brain development. Neurosci Res. 2001 Jun; 40(2):125-32. [PMID 11377750]

2. Hirasawa M, et al. Perinatal abrogation of Cdk5 expression in brain results in neuronal migration defects. Proc Natl Acad Sci USA. 2004 Apr 20; 101(16):6249-54. [PMID 15067135]

Intellectual Property: HHS Reference No. E-293-2009/0 - Research Tool. Patent protection is not being pursued for this technology.

Licensing Contact: Sally Hu, Ph.D., M.B.A.; 301-435-5606; hus@mail.nih.gov

Collaborative Research Opportunity: The National Institute for Dental and Craniofacial Research is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize knockout mice for neurobiological studies. For collaboration opportunities, please contact David Bradley, Ph.D. at bradleyda@nidcr.nih.gov.

Novel Vaccine for Prevention and Treatment of Chlamydia Infection

Description of Technology: The invention provides novel vectors, attenuated pathogens, compositions, methods and kits for preventing and/or treating chlamydia infections.

Chlamydia trachomatis is an obligate intracellular human pathogen with a unique biphasic developmental growth cycle. It's the etiological agent of trachoma, the world's

leading cause of preventable blindness and the most common cause of bacterial sexually transmitted disease. *C. trachomatis* isolates maintain a highly conserved plasmid and naturally occurring plasmidless clinical isolates are rare, implicating its importance in chlamydial pathogenesis. Understanding the plasmid's role in chlamydial pathogenesis at a molecular level is an important objective for the future control of chlamydial infections. The NIAID inventor had studied chlamydia strains in both non-human primate and murine infectious models providing evidence that plasmids play an important role in chlamydial pathogenesis. In addition, the study results of macaque model of trachoma supports the use of plasmid-deficient organisms as novel live-attenuated chlamydial vaccines.

Potential Commercial Applications: Novel live-attenuated chlamydial vaccines.

Competitive Advantages:

• Virulence attenuated vectors that can be used as vaccines against chlamydia.

• Combination of vector with attenuated pathogenic agent improves the stability and replicative capacity of the pathogen.

• Features nucleic acids, attenuated pathogens, compositions, methods and kits to treat and prevent chlamydia infections.

Development Stage:

• In vitro data available

• In vivo data available (animal)

• In vivo data available (human)

• Prototype

Inventor: Harlan D Caldwell (NIAID)

Publications:

1. Song L, et al. Chlamydia trachomatis plasmid-encoded Pgp4 is a transcriptional regulator of virulence associated genes. Infect Immun. 2013 Mar;81(3):636-44. [PMID 23319558]

2. Kari L, et al. A live-attenuated chlamydial vaccine protects against trachoma in nonhuman primates. J Exp Med. 2011 Oct 24;208(11):2217-23. [PMID 21987657]

Intellectual Property: HHS Reference No. E-133-2012/0 -

• US Provisional Application No. 61/753,320 filed 16 Jan 2013

• PCT Application No. PCT/US2014/011799 filed 16 Jan 2014, which published as WO 2014/113541 on 24 Jul 2014

Licensing Contact: Peter Soukas; 301-435-4646; ps193c@nih.gov

Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases, Laboratory of Clinical Infectious Diseases, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize chlamydia vaccine. For collaboration opportunities, please contact Harlan D. Caldwell, Ph.D. at hcaldwell@niaid.nih.gov.

Anti-CD47 Antibodies for the Treatment of Cancer

Summary: Researchers at the National Cancer Institute found that CD47 enhances renewal of breast cancer stem cells, and antibody targeting of CD47 forces these stem cells to differentiate.

Description of Technology: High expression of CD47, a cell surface receptor on several types of cancer cells, has been identified as a 'don't eat me signal' that inhibits their killing by macrophages, cytotoxic T cells, and NK cells. Conversely, the CD47 antibody B6H12 that blocks SIRPα binding enhances macrophage-dependent clearance of tumors in several mouse models, although others have shown that such clearance can be independent of SIRPα signaling.

Cancer stems cells (CSCs) are tumorigenic cells that are difficult to target with conventional chemotherapies due to their undifferentiated state. Stem cells also play an important role in the pathogenesis of cancer. CSCs have been reported to express elevated CD47 levels, but the role of CD47 in directly regulating cancer stem cell function has not been examined.

Researchers at the National Cancer Institute's Laboratory of Pathology found in nonmalignant cells and tissues that the absence of CD47 enhances stem cell renewal *in vitro* and *in vivo* by increasing expression of four stem cell transcription factors (see related technologies below). Conversely, cancer stem cells often express high levels of CD47, and decreasing CD47 is associated with loss of stem cell characteristics. More recently, they discovered methods to force differentiation of breast cancer stem cells by targeting the receptor CD47. These methods disrupt EGF receptor signaling and up-regulate tumor suppressor gene expression in breast cancer stem cells from triple negative breast cancers, but have no effect on normal mammary epithelial cells.

Potential Commercial Applications:

• Treatment for breast cancer and other cancers

• Antibodies for biomedical research

Competitive Advantages: Monoclonal antibodies that directly target CD47-expressing cancers.

Development Stage: Pre-clinical (in vivo)

Inventors: David D. Roberts and Sukhbir Kaur (NCI)

Publication: Kaur S, et al. Role of CD47 in triple negative breast cancer. FASEB J. 2015 April;29(1 Supplement); Abstract 890.5. [http://www.fasebj.org/content/29/1_Supplement/890.5]

Intellectual Property: HHS Reference No. E-263-2014/0 - US Application No. 62/062,675 filed October 10, 2014

Related Technologies:

• HHS Reference No. E-227-2006/5 - US Patent 8,236,313 issued August 7, 2012; US Patent 8,557,788 issued October 15, 2013; US Patent 8,865,672 issued October 21, 2014

• HHS Reference No. E-153-2008/0 - US Patent No. 8,951,527 issued February 10, 2015

• HHS Reference No. E-086-2012/1 - US Patent Application No. 61/735,701 filed December 11, 2012

• HHS Reference No. E-296-2011/0 - Application PCT/US2014/025989 filed March 13, 2014

Licensing Contact: Jaime M. Greene; 301-435-5559; jaime.greene@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute, Center for Cancer Research, Laboratory of Pathology, is seeking statements of capability or interest

from parties interested in collaborative research to further develop, evaluate or commercialize methods to differentiate cancer stem cells. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

Prevention or Treatment of Viral Infections by Inhibition of the Histone Methyltransferases EZH1/2

Description of Technology: Herpes simplex viral infections, including herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2), are exceptionally common worldwide. These viruses establish lifelong persistent infections with cycles of lytic reactivation to produce recurrent diseases including oral and genital lesions, herpetic keratitis/blindness, congenital-developmental syndromes, and viral encephalitis. Infection with HSV-2 increases the rate of human immunodeficiency virus (HIV) transmission in coinfected individuals. DNA replication inhibitors are typically used to treat herpesvirus infections. However, these compounds do not completely suppress infection, viral shedding, reactivation from latency, and the inflammation that contributes to diseases such as keratitis. An unmet need continues to exist for methods of preventing or treating herpesviral infections. The application claims methods of preventing or treating herpesviral infection of a host, comprising administering to the host an effective amount of an inhibitor of the EZH1/2 histone methyltransferase activities. The application is not limited to herpes simplex virus but rather is applicable to other viral infections as well.

Potential Commercial Applications:

- HSV therapeutics
- HSV vaccines

Competitive Advantages:

• Low-cost production

• Ease of synthesis

Development Stage:

• In vitro data available

• In vivo data available (animal)

Inventors: Thomas M. Kristie and Jesse H. Arbuckle (NIAID)

Intellectual Property: HHS Reference E-141-2015/0 - US Provisional Patent Application 62/155,704 filed 01 May 2015

Related Technologies:

• HHS Reference E-275-2008/0 - US Patent Number 8,916,596 issued 23 Dec 2014; US Application No. 14/543,321 filed 17 Nov 2014; PCT Application No. PCT/US2009/051557 filed 23 Jul 2009

• HHS Reference E-184-2010/0 - US Patent Number 8,871,789 issued 28 Oct 2014; PCT Application No. PCT/US2011/044835 filed 21 Jul 2011

Licensing Contact: Peter Soukas; 301-435-4646; ps193c@nih.gov

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Acting Director
Office of Technology Transfer
National Institutes of Health

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